Evaluation of central corneal thickness in patients with dry eye disease in a tertiary eye hospital in Kancheepuram

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ABSTRACT

Background: Dry eye disorder is a disease mainly due to the tear insufficiency which results in eye discomfort and disturbances in vision. Dry eye also affects the ocular dimensions, especially corneal thickness. Central corneal thickness (CCT) assessment plays an important role in refractive surgeries and in the pre-operative assessment of other ocular surgeries. **Aims and Objectives:** This study aims to assess the effect of dry eye disease (DED) on CCT with age- and gender-matched controls. **Materials and Methods:** One hundred and four subjects (52 cases and 52 controls) who attended SRM Medical College and Hospital ophthalmology outpatient department were included in the study. DED was diagnosed with DEQS questionnaire, slit-lamp examination, TFBUT, and Schirmer's test. Pachymetry was used for measuring the CCT of all subjects. Student "t"-test was used to determine the significance of difference between two means. P<0.05 was considered statistically significant. **Results:** In our study, there were 60 female patients and 44 male patients. The ratio of male-to-female was 1:1.3. The CCT among cases was very low (533.19 μm ± 30.05) compared to controls (569.27 μm ± 45.56) and this difference was statistically significant (P<0.05). When subgrouped under gender, the difference in CCT among males between the two groups was statistically significant and it was highly significant among females. When the reduction in CCT among the cases was studied under different age groups, the subjects in the 41–60 years age group had a statistically highly significant difference in CCT between the two groups while it was also significant in other age groups. **Conclusion:** There is a significant decrease in CCT due to DED. Pachymetry for central corneal estimation shall be included in the routine management of dry eye patients so that corneal thinning could be identified earlier and treated with artificial tears or other substitutes.

Key words: Central corneal thickness; Dry eye disease; Pachymetry; Schirmer's test; Tear film breakup time

INTRODUCTION

Cornea is a transparent and avascular structure. It consists of mainly five layers. Corneal epithelium is a stratified squamous type.[1] It consists of five to six layers. Its superficial layers are flattened and deepest layer is columnar cells. Bowman's membrane is made up of acellular mass of condensed collagen fibrils. About 90% of total corneal thickness is stroma. Stroma has collagen fibrils (lamella). Descemet membrane is a strong homogeneous layer which binds to the stroma posteriorly. Endothelium is a single layer hexagonal cell.

The importance of tear film in maintaining a clear cornea has already been accepted. It keeps the cornea moist. Tear film consist of three layers.[2] Outer is lipid layer, then aqueous layer and innermost mucin layer. Lipid layer prevents evaporation and overflow of tears. Aqueous layer forms the main bulk of tear film. Its function is to give atmospheric oxygen to the corneal epithelium, has

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antibacterial substances, and washes away debris. The mucin helps in making the tear film stable.

We can describe dry eye as a state of abnormal tear film which can be due to number of conditions which effects on its stability and changes its composition.[3] According to International Dry Eye Workshop,[4] the dry eye disease (DED) definition included the tear film hyperosmolarity and ocular surface inflammation. An increase in inflammation leads to increase in tear osmolarity. This hyperosmolarity of the tear film results in dehydration of cornea. In normal healthy individual, the aqueous layer of the tear film is isotonic or mildly hypertonic. Hypertonic solution decreases corneal thickness. Hence, as the tear production goes down, there is an increase in tear film osmolarity and the cornea becomes thin.

Corneal endothelial disease is said to have an impact on central corneal thickness (CCT). Corneal thickness is helpful in diagnosing corneal diseases and evaluating endothelial pump function. Therefore, measurement of the thickness of the cornea along with its shape and power is quite helpful in diagnosing corneal diseases and deciding corneal surgery for vision correction.

CCT can be used as an important factor to predict the survival of corneal graft.[5] CCT is good predictor for the development of primary open-angle glaucoma in OHTS subjects.[6]

DED is believed to be caused by tear deficiency, excessive evaporation of tear, and an unstable tear film. It is said to cause symptoms and also impair vision. DED damages the ocular surface. Since DED has an etiology which is not very clear, the criteria to diagnosis of DED are also not very clear and standardized.

DED is increasing due to aging, excessive smartphone, and electronic devices uses. Female sex, collagen vascular disease,[7] hay fever, depression drugs, contact lens use,[8] prolonged screen time, and smoking are risk factors for severe DED. Glaucoma medications may also contribute to ocular surface disease and development of dry eye. People wearing contact lens has changes in their ocular surface. It is more evident in keratoconus[9] subjects who are contact lens wearer. Evident central corneal thinning has been reported in keratoconjunctivitis sicca patients.[10]

With the increasing digital devise usage for both work and play in these times, large numbers of people are getting affected by DED worldwide. Most of the people who have undiagnosed DED usually have a decreased quality of vision, in turn lead to poor work productivity.

Aims and objectives

The purpose of this study was to compare the CCT in DED patients with age- and gender-matched controls.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Ophthalmology Department of SRM Medical College and Hospital for a period of one year spanning from August 2019 to July 2020. The study was approved by the Institutional Ethics Committee. DED patients who attended SRM Medical College and Hospital ophthalmology OPD were included in our study. Patients with rheumatoid arthritis, diabetes mellitus, uveitis, glaucoma, increased IOP, eyelid disorders, ptosis, and any corneal disease were excluded from the study. Patients with a history of previous eye surgery were also excluded from the study. Age- and gender-matched controls were selected from the population diagnosed without DED who visited ophthalmology outpatient department of SRM Medical Hospital.

Sample size

According to Ali et al., study,[11] considering the mean (μ_1) and standard deviation (σ_1) of CCT in controls as 561.1 μm$\pm$28.6, and mean (μ_2) and standard deviation (σ_2) of CCT in DED patients as 542.4 μm$\pm$38.1, at 95 % confidence interval (Z_{1-al2}=1.96), with 80 % power ($Z_{1-\beta}$=0.84), the sample size is calculated as N = $(Z_{1-al2}+Z_{1-\beta})^2 * 2 * \sigma^2/(\mu_1-\mu_2)^2$=(1.96 + 0.84)$^2 * 33.35^2/(561.1-542.4)^2$=50. Considering a 5% non-response rate, the sample size required for each group is 52 and the total sample size for the study is 104.

Diagnosis of dry eye

The dry eye was diagnosed with the following steps. Patients with either subjective or objective findings were considered to DED.

a. Dry eye-related quality of life score (DEQS) questionnaire: DEQ score of more than 15 was considered to have dry eye.
b. Slit-lamp examination: This was done to exclude other ocular disorder and to proceed with TBUT.
c. TBUT: First dark spot $\leq$5 s was considered as diagnosis of DED
d. Schirmer's test 1: Patients who had a Schirmer's test score $\leq$10 mm in 5 min were considered to have dry eye.

Study procedure

After obtaining informed consent from the patient, a detailed history was taken. In ocular examination, best-corrected visual acuity, intraocular pressure, anterior segment examination by slit-lamp biomicroscopy, and fundus examination were done. We recorded subjective

symptoms of our study group using DEQS.[12] All these patients then underwent tear film breakup time (TFBUT), keratoconjunctival staining, and Schirmer test. Patients were classified as DED and non-DED using the Asian Dry Eye Society 2016 diagnostic criteria.[13] These criteria include two positive points: The presence of subjective symptoms and decreased TFBUT≤5 s. After this, the DED patients were divided into mild to severe on the basis of vital staining.

All patients in our study underwent subjective symptoms assessment using the DEQ questionnaire. This helped us in evaluating them. To diagnose DED, a cutoff value of DEQS >15 was used in our study.

With the help of fluorescein dye, TFBUT was evaluated in our patients. We noted the time interval between the last blink and the appearance of the first dark spot on the cornea. We used TFBUT≤5 s to make diagnosis of DED. Using Schirmer's test strips, we did Schirmer's test without topical anesthesia. Schirmer's test strips were placed on the outer third of the temporal lower conjunctival fornix for 5 min. Then after removing it, the value was recorded in millimeter. Value less than 10 mm was diagnosed as dry eye.

CCT was performed using ultrasound pachymeter. There are different methods of evaluating corneal thickness.[14,15] It includes ultrasonic pachymetry, optical slit-lamp pachymetry, specular microscopy, and confocal microscopy. Each of these methods has different disadvantages. Ultrasound pachymetry requires corneal contact whereas Orbscan system is a non-contact method. Few studies suggest that Orbscan has an accurate and precision almost equal to ultrasonic pachymetry.[16,17] All subjects were examined by the same examiner. We used a mean of three successive measurements.

Combination of diagnostic tests helped us in diagnosing dry eye syndrome more efficiently. Few dry eye subjects had no symptoms but a positive objective finding of dry eye. Others had severe symptoms but without dry eye findings. The DEDS questionnaire consists of 15 questions regarding ocular symptoms and their impact on daily life. DEDS is very useful in evaluating the effects of DED syndrome on the daily life of patients including its effect on mental health. Hence, subjects were asked to score their general ocular symptoms and quality of life on a scale of 1–6, where 6 showed a poor quality of life and 1 showed a very good quality of life.[18]

Statistical analysis

Data were entered into Microsoft Excel version Office 16 and analyzed using IBM Statistical Package for the Software Solutions version 21. Descriptive statistics were represented by mean and standard deviation. Student's "t"-test was used to determine the significance of difference between two means. P<0.05 was considered statistically significant.

RESULTS

Fifty-two subjects diagnosed of DED (cases) and 52 subjects diagnosed without DED (controls) were included in the study. A total of 44 males and 60 females participated in the study with same distribution in both groups. The age of the subjects including both groups varied from a minimum of 27 years to a maximum of 75 years with a mean of 50.9 years.

The mean age of the two groups had no statistically significant difference (p > 0.05). When compared the mean age of males and females in the two groups separately, there was no significant difference between cases and controls (p > 0.05). The age and gender are almost matched between cases and controls, as shown in Table 1.

The CCT among cases was very low (533.19 micometer±30.05) compared to controls (569.27 μm±45.56) and this difference was statistically significant (P<0.05). When subgrouped under gender, the difference in CCT among males between the two groups was statistically significant and it was highly significant among females, as shown in Table 2.

When the reduction in CCT among the cases was studied under different age groups, the subjects in the 41–60 years age group had a statistically highly significant difference in CCT between the two groups while it was also significant in other age groups, as shown in Table 3.

DISCUSSION

The mean age of the subjects in cases and control groups was 51.62 and 50.35 years, respectively, which is very comparable. Similarly, the mean age among males and females in both groups was also comparable. This study aimed to assess the effect of DED on CCT by comparing with age- and gender-matched controls. CCT plays an important role in refractive surgeries and intraocular pressure assessment in glaucoma cases.

The study showed that the CCT was significantly reduced in patients with DED when compared with normal eyes of age- and gender-matched population. The mean CCT among the cases was 533.19 μm ± 30 μm and 569.27±45 μm in the control group, and the difference in CCT between the two groups was about 36 μm. This finding almost correlates with many corneal morphometric studies

Table 1: Comparison of demographic data of dry eye disease patients and control groups

Age (years)	Cases		Controls		P value "t" test	Significance
	Mean	S.D.	Mean	S.D.		
Overall	51.62	13.99	50.35	10.31	0.6	NS
Males	49.73	14.38	48.09	11.76	0.682	NS
Females	53.00	13.77	52.00	8.94	0.74	NS

Table 2: Comparison of CCT (ultrasound pachymetry) among dry eye disease patients and control groups

CCT (μm)	Cases		Controls		P value "t" test	Significance
	Mean (μm)	S.D.	Mean (μm)	S.D.		
Overall	533.19	30.05	569.27	45.56	0.001	HS
Males	534.95	34.68	567.77	46.70	0.011	S
Females	531.90	26.70	570.37	45.47	0.001	HS

CCT: Central corneal thickness

Table 3: Comparison of CCT among cases and controls in different age groups

CCT (μm)	Cases		Controls		P value "t" test	Significance
	Mean (μm)	S.D.	Mean (μm)	S.D.		
21–40 years	534.92	29.74	561.00	23.12	0.031	S
41–60 years	528.46	30.45	571.29	44.41	0.001	HS
>60 years	539.27	30.47	569.89	33.60	0.035	S

CCT: Central corneal thickness

which reported that the dry eye can cause significant decrease in CCT values.

Liu and Pflugfelder[19] (1999) showed that the mean difference in CCT between normal and dry eyes was approximately 35 μm; the CCT was 571 μm±28 and 534 μm±34 μm in normal and dry eye, respectively. Sanchis-Gimeno et al.,[20] (2005) showed that the CCT in normal eyes was 558 μm±30 μm, while it was 532 μm±34 μm in dry eyes and the mean difference between the two groups was 26 μm. Sanchis-Gimeno et al.,[21] (2006) compared normal and dry eyes to estimate the differences in ocular dimensions and showed CCT of 549 μm±34 μm in normal eyes and 527 μm±30 μm in dry eyes with a difference in CCT of 22 μm between two groups. Ali et al.,[11] (2017) estimated the mean CCT in cases group as 536.5 μm, while it was 561.3 μm in the control group, and the difference was about 25 μm. Another study by Sanchis-Gimeno et al.,[7] (2004) done in postmenopausal women, observed 14 μm difference in mean CCT between normal and dry eyes. The mean CCT among postmenopausal women with dry eyes was 533.10±4.74 μm while it was 547.63±15.11 μm in age-matched control women. Gunes et al.,[22] reported the mean CCT as 529±32.8 μm and 556±27.5 μm in dry and normal eyes of rheumatoid arthritis patients, respectively, with a difference in CCT of 27 μm between normal and dry eyes.

When CCT values were analyzed in subgroups of age and gender between cases and controls, there was a significant difference between the two groups. The difference in CCT among females between cases and controls was 38 μm (531.9±26.7 μm vs. 570.37±45.47 μm) which was highly significant. Among males, the CCT was 534.95±34.68 μm among cases compared to 567.77±46.7 μm in controls and the difference was 32 μm which was also statistically significant. The effect of dry eye on CCT was more in females compared to males. Ali et al.,[11] also showed similar results with a difference of 19 μm in males (561.9±28.6 μm vs. 542.4±38.1 μm) and 29 μm in females (561.4±27.2 μm vs. 532.6±37.1 μm).

Similarly, the CCT difference was very evident between normal and dry eyes in all age groups. The difference was high in 40–60 years age group which was 42 μm followed by >60 years age group which had 30 μm and about 6 μm in 20–40 years age group. The results are almost similar with Ali et al.,[11] which also presented significant difference in CCT in all age groups between cases and controls.

The corneal thinning in dry eye syndrome is actually due to increase in tear film evaporation or increased osmolarity of tear fluid. It causes a decrease in tear film thickness which normally ranges from 3 to 40 μm. This hyperosmolar tear film activates the inflammatory cascade. This activation of inflammatory cascade stimulates the epithelial cells to produce high amounts of cytokines and matrix metallopeptidase (MMP). Several studies have shown that these inflammatory events lead to apoptotic

death of surface epithelial cells of cornea.[23] There is evidence to show that excessive apoptosis or shedding of the surface epithelium, if sustained and not compensated for any epithelial cycling, ultimately causes corneal epithelial thinning.[24]

Another theory for corneal thinning in DED is due to imbalance between MMP-1 and tissue inhibitor of MMP-1. MMP-1 is responsible for the degradation of extracellular matrix in the stroma of cornea. This imbalance is due to elevated level of cytokines which subsequently leads to accumulation of collagenases in the cornea, causing destructive keratolysis and corneal thinning.[25]

These evidence and studies promoted the use of tear substitute to protect the corneal from thinning in DED patients. Karadayi et al.,[26] have shown in their study that there was increase in CCT after the treatment of DED patients with artificial tear drop. This study supports the concept of doing pachymetry in routine management of DED patients.

Limitations of the study

Our study was a cross sectional study with a relative small sample size. These findings need to be confirmed in future studies.

CONCLUSION

DED is one of the most common causes of ocular disease and can lead to lifelong visual discomfort and impairment. Therefore, to make DED, an avoidable cause of visual discomfort, more and more emphasis should be given on doing corneal pachymetry in these patients. Our findings showed that CCT was thinner in dry eye patients, especially female dry eye patient. Hence, along with evaluation of dry eye tests, pachymetry is also important in ophthalmic examinations and should be done in DED patients. This study supports the concept of doing pachymetry in routine management of dry eye disease.

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RH – Participated in acquisition of data, research article concept, and participated in data collection and analysis; **SANA –** Participated in acquisition of data and drafting the manuscript, participated in data collection and analysis, performed the statistical analysis, interpretation, and manuscript editing and manuscript review; and **SKT –** Literature review, data analysis, and interpretation.

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